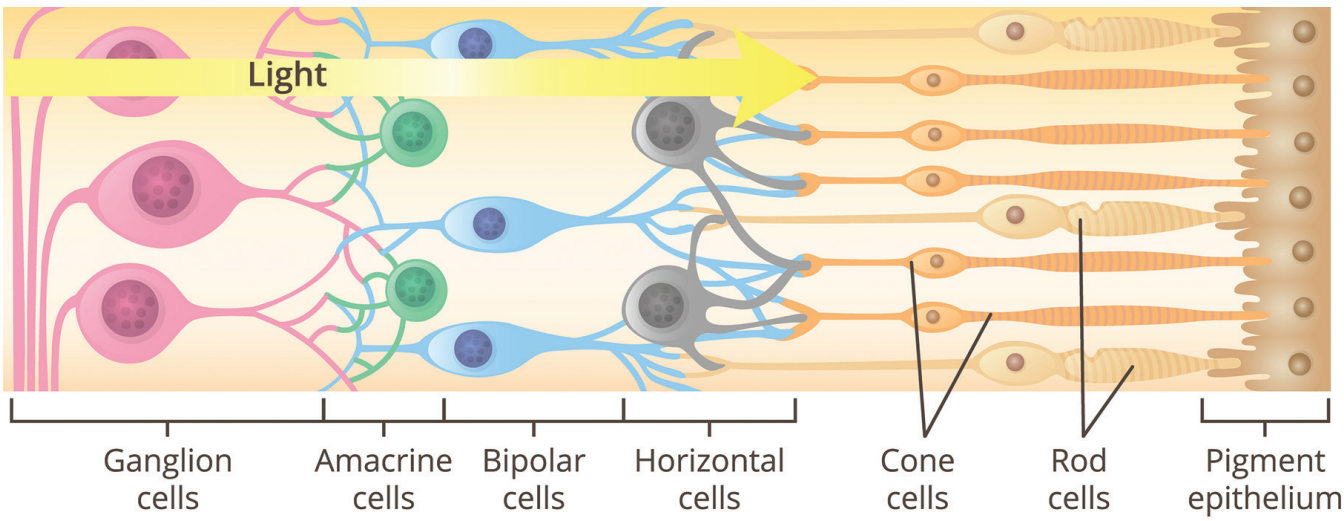
GENE THERAPY FOR INHERITED RETINAL DISEASE: THE PIPELINE

The field of inherited retinal disease research is exploding with more than 30 therapies under investigation for Leber congenital amaurosis, retinitis pigmentosa, Stargardt disease, cone and cone-rod dystrophies, achromatopsia, choroideremia, Usher syndrome, and others. Although many still rely on traditional AAV vectors, several novel mechanisms of action and delivery methods hold promise for improved efficacy and safety and, potentially, gene agnostic treatment. Here, we provide a snapshot of the pipeline to help you educate patients—and foster hope that therapies may soon be within reach for some conditions.

- The Staff of *Retina Today*



Ganglion Cells

Retinitis Pigmentosa
RTx-015 (Ray Therapeutics)
BS01 (Bionic Sight)
GS030-DP/GS030-MD (GenSight Biologics)
KIO-301 (Kiora Pharmaceuticals)

Bipolar Cells

Stargardt Disease/Retinitis Pigmentosa
MCO-010 (Nanoscope)

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Cone/Rod Cells

Achromatopsia
AAV8.hCNGA3 (STZ Eyetrial)

Batten Disease
NGN-101 (Neurogene)
TTX-381 (Tern Therapeutics)

Leber Congenital Amaurosis
ATSN-101 (Atsena Therapeutics)
OPGx-001 (Opus Genetics)
Sepofarsen (Sepul Bio)
rAAV8.hRKp.AIPL1 (MeiraGTx)

Stargardt Disease
OCU410ST (Ocugen)
ACDN-01 (Ascidian Therapeutics)
VG801 (VeonGen)
SB-007 (Splice Bio)

Retinitis Pigmentosa
Iaru-zova (Beacon Therapeutics)
rAAV.hPDE6A (STZ Eyetrial)
AAV2/5-hPDE6B (eyeDNA Therapeutics/Coave Therapeutics)
SPVN06 (SparingVision)
VP-001 (PYC Therapeutics)
VG901 (VeonGen)
OCU400 (Ocugen)
AAV5-hRKp.RPGR (Janssen/Johnson & Johnson)

Usher Syndrome
AAVB-081 (AAVantgarde Bio)
Ultevursen (Sepul Bio)

X-Linked Retinoschisis
ATSN-201 (Atsena Therapeutics)

GENE	TREATMENT AGENT (SPONSOR)	TREATMENT STRATEGY	DELIVERY METHOD	TRIAL ID	PHASE	STATUS	PRIMARY COMPLETION
Leber Congenital Amaurosis							
CEP290	QR-110 (Sepofarsen, Sepul Bio)	Alter splicing error; antisense oligonucleotides	Intravitreal	NCT06891443	3	Recruiting	November 2027
GUCY2D	AAV8-GRK1-GUCY2D (ATSN-101, Atsena Therapeutics)	Gene replacement	Subretinal	NCT03920007	1/2	Active, not recruiting	May 2023
LCA5	AAV8-hLCA5 (OPGx-001, Opus Genetics)	Gene replacement	Subretinal	NCT05616793	1/2	Recruiting	December 2024
AIPL1	rAAV8.hRKp.AIPL1 (MeiraGTx)	Gene replacement	Subretinal	Under investigation in the United Kingdom			
Retinitis Pigmentosa/Rod-Cone Dystrophy							
RPGR	AAV5-hRKp.RPGR (Janssen/Johnson & Johnson)	Gene replacement	Subretinal	NCT04671433	3	Complete	
				NCT04794101	3	Active, not recruiting	September 2029
Gene agnostic	OCU400 (Ocugen)	Overexpression of NR2E3	Subretinal	NCT06388200	3	Recruiting	June 2025
Gene agnostic	MCO-010 (Nanoscope)	Optogenetics	Intravitreal	NCT04945772	2b	Complete	
Gene agnostic	KIO-301 (Kiora Pharmaceuticals)	Photoswitch	Intravitreal	NCT06628947	2	Not yet recruiting	March 2026
RPGR	rAAV2tYF-GRK1-RPGR (Iaru-zova; AGTC-501, Beacon Therapeutics)	Gene replacement	Subretinal	NCT04850118	2/3	Recruiting	August 2025
				NCT03316560	1/2	Active, not recruiting	November 2023
				NCT06333249	1/2	Active, not recruiting	April 2023
PDE6A	rAAV.hPDE6A (STZ Eyetrial)	Gene replacement	Subretinal	NCT04611503	1/2a	Active, not recruiting	July 2027
PDE6B	AAV2/5-hPDE6B (eyeDNA Therapeutics/Coave Therapeutics)	Gene replacement	Subretinal	NCT03328130	1/2	Recruiting	December 2029
Gene agnostic; *RHO, PDE*	AAV-RdCVF-RdCVFL (SPVN06, SparingVision)	Overexpression of rod-derived cone viability factor; a cone neurotrophic factor	Subretinal	NCT05748873	1/2	Recruiting	March 2025
Gene agnostic	rAAV2.7m8-CAG-ChrimsonR-tdTomato (GS030-DP, GS030-MD, GenSight Biologics)	Optogenetics and visual interface stimulating glasses	Intravitreal	NCT03326336	1/2a	Recruiting	December 2022
Gene agnostic	AAV2-CAG-ChronosFP (BS01, Bionic Sight)	Optogenetics	Intravitreal	NCT04278131	1/2	Recruiting	December 2024
CNGA1	AAV2.NN-CNGA1 (VG901, VeonGen)	Gene replacement	Intravitreal	NCT06291935	1b	Recruiting	April 2026
Gene agnostic	RTx-015 (Ray Therapeutics)	Optogenetics	Intravitreal	NCT06460844	1	Recruiting	May 2026
PRPF31	VP-001 (PYC Therapeutics)	Gene replacement	Intravitreal	NCT06455826	1	Recruiting	November 2025
				NCT06852963	1/2	Not yet recruiting	June 2027
Stargardt Disease							
Gene agnostic	MCO-010 (Nanoscope)	Optogenetics	Intravitreal	NCT05417126	2	Complete	
ABCA4	AAV5-hRORA (OCU410ST, Ocugen)	Regulates pathways in oxidative stress and lipofuscin formation	Subretinal	NCT05956626	1/2	Recruiting	October 2025
ABCA4	VG801 (VeonGen)	Gene replacement	Subretinal	NCT07002398	1/2	Recruiting	May 2026
ABCA4	SB-007 (Splice Bio)	Gene replacement	Subretinal	NCT06942572	1/2	Recruiting	October 2028
ABCA4	ACDN-01 (Ascidian Therapeutics)	Exon-editing RNA	Subretinal	NCT06467344	1/2	Recruiting	August 2030
X-Linked Retinoschisis							
RS1	AAV.SPR-hGRK1-hRS1syn (ATSN-201, Atsena Therapeutics)	Gene replacement	Subretinal	NCT05878860	1/2	Recruiting	October 2025
Usher Syndrome							
USH2A	Ultevursen (Sepul Bio)	Antisense oligonucleotide; induces exon 13 skipping	Intravitreal	NCT06627179	2b	Recruiting	December 2027
MYO7A	AAVB-081 (AAVantgarde Bio)	Gene replacement	Subretinal	NCT06591793	1/2	Recruiting	July 2025
Achromatopsia							
CNGA3	AAV8.hCNGA3 (STZ Eyetrial)	Gene replacement	Subretinal	NCT02610582	1/2	Active, not recruiting	June 2027
Batten Disease							
CLN2	TTX-381 (Tern Therapeutics)	Gene replacement	Subretinal	NCT05791864	1/2	Recruiting	July 2026
CLN5	NGN-101 (Neurogene)	Gene replacement	Intracerebroventricular and intravitreal	NCT05228145	1/2	Active, not recruiting	November 2028